

Claims

1. A recombinant host cell capable of making a polyketide using a starter unit, wherein the recombinant host cell is derived from a native host cell by modification with an expression vector, and wherein:

(a) the native host cell is incapable of producing the starter unit and the expression vector expresses one or more proteins that produce the starter unit, or

(b) the native host cell produces the starter unit and the expression vector overexpresses one or more proteins whose expression results in increased production of the starter unit.

2. The host cell of Claim 1, wherein the expression vector expresses or overexpresses the atoAD enzyme.

3. The host cell of Claim 1 or 2, wherein the expression vector expresses or overexpresses a positive transcription regulator that increases the expression of the atoAD enzyme.

4. The host cell of Claim 3, wherein the positive transcription regulator is the atoC protein.

5. The host cell of Claim 1, further modified to express methylmalonyl-CoA mutase and methylmalonyl-CoA epimerase.

6. The host cell of Claim 1 wherein the starter unit is selected from the group consisting of acetyl CoA, butyryl CoA, 3-fluoropropionyl CoA, 3-chloropropionyl CoA, 3,3,3-trifluoropropionyl CoA, 3-hydroxypropionyl CoA, fluoroacetyl CoA, lactyl CoA, (methylthio)acetyl CoA, chloroacetyl CoA, glycolyl CoA, 4-chlorobutyryl CoA, 2-methylbutyryl CoA, and valeryl CoA.

7. The host cell of Claim 6 wherein the starter unit is selected from the group consisting of acetyl CoA, butyryl CoA, (methylthio)acetyl CoA, 4-chlorobutyryl CoA, 2-methylbutyryl CoA, and valeryl CoA.

8. The host cell of Claim 6 wherein the starter unit is butyryl CoA or (methylthio)acetyl CoA.
9. The host cell of Claim 1 that is an *Escherichia coli* host cell.
10. The host cell of Claim 2 that is an *Escherichia coli* host cell.
11. The host cell of Claim 1 that is a yeast host cell.
12. The host cell of Claim 1, wherein the polyketide is synthesized by a modular polyketide synthase (PKS).
13. The host cell of Claim 1, wherein the polyketide is an analog of 6-deoxyerythronolide B (6-dEB) modified by replacement of the propionate starter unit.
14. The host cell of Claim 13, wherein the polyketide is selected from the group consisting of 14-desmethyl-6-dEB, 15-methyl-6-dEB, 15-fluoro-6-dEB, 15-chloro-6-dEB, 15-trifluoro-6-dEB, 15-hydroxy-6-dEB, 14-desmethyl-14-fluoro-6-dEB, 14-hydroxy-6-dEB, 14-desmethyl-14-(methylthio)-6-dEB, 14-desmethyl-14-chloro-6-dEB, 14-desmethyl-14-hydroxy-6-dEB, 15-(chloromethyl)-6-dEB, 14-ethyl-6-dEB, and 15-ethyl-6-dEB.
15. The host cell of Claim 13 wherein the polyketide is 15-methyl-6-dEB or 14-desmethyl-14-(methylthio)-6-dEB.
16. The host cell of Claim 5 which has been further modified to overexpress a B12 transporter gene.
17. The host cell of Claim 1, further modified to express propionyl-CoA carboxylase.
18. The host cell of Claim 17, further modified to overexpress a biotin ligase enzyme.

19. The host cell of Claim 18 wherein the biotin ligase enzyme is encoded by the *birA* gene.

20. A method for producing an analog of 6-deoxyerythronolide B (6-dEB) modified by replacement of the propionate starter unit in a host cell of Claim 1, comprising culturing the host cell under conditions wherein the analog of 6-dEB is produced.